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# SEARCH REQUEST FORM

Scientific and Technical Information Center 10/10/03

Requester's Full Name: Rebecca Cook Examiner #: _____ Date: 9/15/03
Art Unit: 1614 Phone Number 308 4724 Serial Number: 10/070,462
Mail Box and Bldg/Room Location: 1614 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

**********

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Rush Search Approved TK Page SPE, AU1616

Inventors (please provide full names): David Brown

Earliest Priority Filing Date: 9/16/99

*For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

- Please provide structures for ursolic acid + retinoic acid
- Search method for increasing lipid content of epidermal keratinocytes using ursolic acid
- Print all abstracts in full
- What is known use of ursolic acid
- Search phospholiped bilayer membrane liposome in topical preparations; encapsulating

- { ursolic acid / retinoid / steroid } each to increase ceramide lipid " " free fatty acid

Claims are attached

Thanks you
Rebecca Cook

| STAFF USE ONLY | Type of Search | Vendors and cost where applicable |
|---|---|---|
| Searcher: | NA Sequence (#) | STN 330.95 |
| Searcher Phone #: | AA Sequence (#) | Dialog |
| Searcher Location: | Structure (#) | Questel/Orbit |
| Date Searcher Picked Up: 9/24 | Bibliographic | Dr. Link |
| Date Completed: 9/24 | Litigation | Lexis/Nexis |
| Searcher Prep & Review Time: 30 | Fulltext | Sequence Systems |
| Clerical Prep Time: | Patent Family | WWW/Internet |
| Online Time: 30 | Other | Other (specify) |

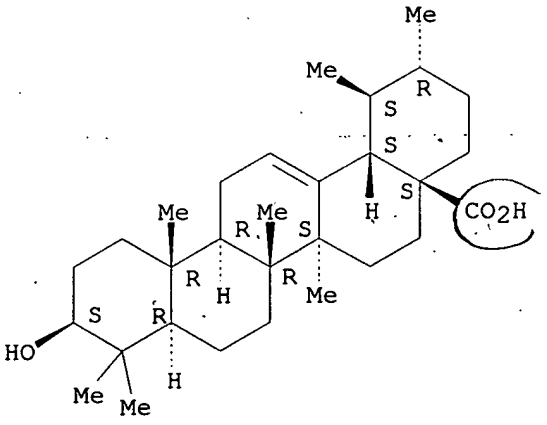
PTO-1590 (8-01)

Structure of ursolic acid



L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN 77-52-1 REGISTRY
CN Urs-12-en-28-oic acid, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Urs-12-en-28-oic acid, 3.beta.-hydroxy- (8CI)
OTHER NAMES:
CN (+)-Ursolic acid
CN .beta.-Ursolic acid
CN 3.beta.-Hydroxyurs-12-en-28-oic acid
CN Bungeolic acid
CN Malol
CN Merotaine
CN NSC 167406
CN NSC 4060
CN Prunol
CN **Ursolic acid**
CN Urson
FS STEREOSEARCH
DR 209545-05-1
MF C30 H48 O3
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, DDFU, DETHERM*, DRUGU, EMBASE, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, PROMT, RTECS*, SPECINFO, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (+).




514/577

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

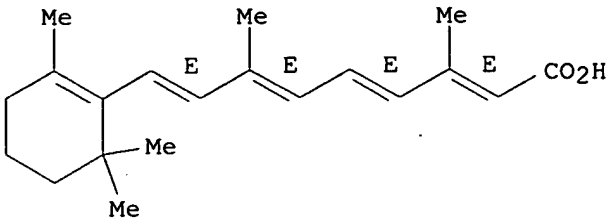
1755 REFERENCES IN FILE CA (1907 TO DATE)
30 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1765 REFERENCES IN FILE CAPLUS (1907 TO DATE)
18 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

Structure of Retinoic acid



L8 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN 302-79-4 REGISTRY
CN Retinoic acid (6CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Retinoic acid, all-trans- (8CI)
OTHER NAMES:
CN (all-E)-3,7-Dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2,4,6,8-nonatetraenoic acid
CN .beta.-Retinoic acid
CN 2,4,6,8-Nonatetraenoic acid, 3,7-dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-, (all-E)-
CN 3,7-Dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2,4,6,8-nonatetraenoic acid
CN Aberel
CN AGN 100335
CN Airol
CN Aknoten
CN all-(E)-Retinoic acid
CN all-trans-.beta.-Retinoic acid
CN all-trans-Retinoic acid
CN all-trans-Tretinoin
CN all-trans-Vitamin A acid
CN ATRA
CN Atragen
CN Cordes Vas
CN Dermairol
CN Epi-Aberel
CN Eudyna
CN NSC 122578
CN NSC 122758
CN Renova
CN Retacnyl
CN Retin A
CN Ro 1-5488
CN trans-Retinoic acid
CN Tretin M
CN Tretinoin
CN Vesanoid
CN Vesnaroid
CN Vitamin A acid
CN Vitamin A acid, all-trans-
CN Vitamin A1 acid, all-trans-
FS STEREOSEARCH
DR 7005-78-9, 56573-65-0, 187175-63-9
MF C20 H28 O2
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGNL, DRUGU, DRUGUPDATES, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Double bond geometry as shown.




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

11957 REFERENCES IN FILE CA (1907 TO DATE)
316 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
11979 REFERENCES IN FILE CAPLUS (1907 TO DATE)
23 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

5,414/558,560

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=> d que
L7            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "URSOLIC ACID"/CN
L9         1767 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7
L18           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L9 OR URSOLIC ACID) AND
                (PHOSPHOLIP? AND (BILAY? OR LAY? OR MEMBRAN? OR LIPOSO?))

=> d ibib abs hitind hitstr l18 1-3

L18  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2001:185567  HCAPLUS
DOCUMENT NUMBER:          134:242647
TITLE:                    Compositions containing ursolic acid
                          and methods for modification of skin lipid content
INVENTOR(S):              Brown, David A.; Yarosh, Daniel B.
PATENT ASSIGNEE(S):       Applied Genetics Incorporated Dermatics, USA
SOURCE:                   PCT Int. Appl., 41 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND  DATE          APPLICATION NO.  DATE
     ------------------  ----  --------      ---------------  --------
     WO 2001017523        A1   20010315      WO 2000-US24659  20000908
         W:  AU, CA, CN, IL, JP, KR, US
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE
     EP 1210075           A1   20020605      EP 2000-961668   20000908
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI, CY
     JP 2003508486        T2   20030304      JP 2001-521314   20000908
PRIORITY APPLN. INFO.:                    US 1999-153378P  P  19990910
                                          WO 2000-US24659  W  20000908
AB   The topical use of ursolic acid compds. to alter the
     lipid content of mammalian skin is disclosed.  The compds. can be
     encapsulated in liposomes and administered in this form to the
     skin in, for example, a lotion or a gel.  The compds. are effective in,
     among other things, reducing the effects of aging, photoaging, and skin
     atrophy, including skin atrophy resulting from the topical use of
     retinoids and/or steroids.  Compns. comprising a ursolic
     acid compd. in combination with another therapeutically active
     topical compds., such as, a retinoid or a steroid, are also disclosed.
IC   ICM  A61K031-19
CC   63-6 (Pharmaceuticals)
     Section cross-reference(s): 1, 2, 62
ST   topical ursolic acid lipid skin disease
IT   Skin, disease
        (atrophy; compns. contg. ursolic acid compds. for
        modification of skin lipid content in treatment of skin disorders)
IT   Acne
     Preservatives
        (compns. contg. ursolic acid compds. for
        modification of skin lipid content in treatment of skin disorders)
IT   Ceramides
```

Fatty acids, biological studies
Lipids, biological studies
**Phospholipids**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(compns. contg. **ursolic acid** compds. for modification of skin lipid content in treatment of skin disorders)

IT Retinoids
Steroids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. contg. **ursolic acid** compds. for modification of skin lipid content in treatment of skin disorders)

IT Skin, disease
(dry; compns. contg. **ursolic acid** compds. for modification of skin lipid content in treatment of skin disorders)

IT Skin
(epidermis; compns. contg. **ursolic acid** compds. for modification of skin lipid content in treatment of skin disorders)

IT Drug delivery systems
(gels; compns. contg. **ursolic acid** compds. for modification of skin lipid content in treatment of skin disorders)

IT Skin, disease
(ichthyosis; compns. contg. **ursolic acid** compds. for modification of skin lipid content in treatment of skin disorders)

IT Drug delivery systems
(**liposomes**; compns. contg. **ursolic acid** compds. for modification of skin lipid content in treatment of skin disorders)

IT Drug delivery systems
(lotions; compns. contg. **ursolic acid** compds. for modification of skin lipid content in treatment of skin disorders)

IT Skin, disease
(photoaging; compns. contg. **ursolic acid** compds. for modification of skin lipid content in treatment of skin disorders)

IT Aging, animal
(skin; compns. contg. **ursolic acid** compds. for modification of skin lipid content in treatment of skin disorders)

IT Drug delivery systems
(topical; compns. contg. **ursolic acid** compds. for modification of skin lipid content in treatment of skin disorders)

IT **77-52-1**, **Ursolic acid** 464-99-3, Lupane 465-99-6, Hederagenin 471-53-4, 18.beta.-Glycyrrhetic acid 472-15-1, Betulinic acid 473-98-3, Betulin 508-02-1, Oleanolic acid 545-46-0, Uvaol 545-48-2, Erythrodiol 4547-24-4, Corosolic acid 5697-56-3, Carbenoxolone 14226-18-7, Glycyrrhetol 53155-25-2, Euscapic acid 329768-05-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. contg. **ursolic acid** compds. for modification of skin lipid content in treatment of skin disorders)

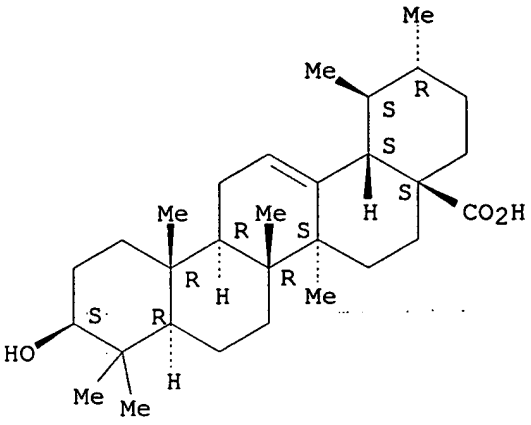
IT 24634-61-5, Potassium sorbate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preservative; compns. contg. **ursolic acid** compds. for modification of skin lipid content in treatment of skin disorders)

IT **77-52-1**, **Ursolic acid**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. contg. **ursolic acid** compds. for modification of skin lipid content in treatment of skin disorders)

RN 77-52-1 HCAPLUS
CN Urs-12-en-28-oic acid, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).




REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:710583 HCAPLUS
DOCUMENT NUMBER: 134:38989
TITLE: Determination of the **phospholipid**/lipophilic compounds ratio in **liposomes** by thin-**layer** chromatography scanning densitometry
AUTHOR(S): Rodriguez, S.; Cesio, M. V.; Heinzen, H.; Moyna, P.
CORPORATE SOURCE: Catedra de Farmacognosia y Productos Naturales, Facultad de Quimica, Universidad de la Republica, Montevideo, Urug.
SOURCE: Lipids (2000), 35(9), 1033-1036
CODEN: LPDSAP; ISSN: 0024-4201
PUBLISHER: AOCS Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The detn. of the ratio of **phospholipid**/lipophilic compds. in **liposomes** was achieved after thin-**layer** chromatog. (TLC) by measuring the spot intensities of dipalmitoyl phosphatidylcholine and the lipophilic compd. The **liposome** components under study were sepd. on one TLC plate, developed in two steps, and detected after charring the plate with specific visualization reagents. The method shows good reproducibility and provides a simple way to quantify the level of lipophilic compd. incorporated in the **liposome bilayer**

CC 9-3 (Biochemical Methods)
ST **phospholipid liposome** ratio TLC dipalmitoyl phosphatidylcholine **membrane bilayer**
IT **Membrane**, biological

(**bilayer**; detn. of **phospholipid**/lipophilic compds. ratio in **liposomes** by thin-**layer** chromatog. scanning densitometry)

IT TLC (thin **layer** chromatography)
(detn. of **phospholipid**/lipophilic compds. ratio in **liposomes** by thin-**layer** chromatog. scanning densitometry)

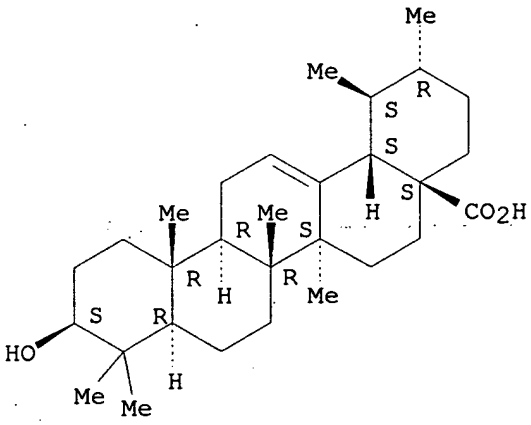
IT **Phospholipids**, biological studies
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(detn. of **phospholipid**/lipophilic compds. ratio in **liposomes** by thin-**layer** chromatog. scanning densitometry)

IT 57-88-5, Cholesterol, analysis 63-89-8, DPPC **77-52-1**, **Ursolic acid** 127-22-0, Taraxerol 473-98-3, Betulin 545-46-0, Uvaol 545-47-1, Lupeol
RL: ANT (Analyte); PEP (Physical, engineering or chemical process); PRP (Properties); ANST (Analytical study); PROC (Process)
(detn. of **phospholipid**/lipophilic compds. ratio in **liposomes** by thin-**layer** chromatog. scanning densitometry)

IT **77-52-1**, **Ursolic acid**
RL: ANT (Analyte); PEP (Physical, engineering or chemical process); PRP (Properties); ANST (Analytical study); PROC (Process)
(detn. of **phospholipid**/lipophilic compds. ratio in **liposomes** by thin-**layer** chromatog. scanning densitometry)

RN 77-52-1 HCAPLUS
CN Urs-12-en-28-oic acid, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).




REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:570998 HCAPLUS
DOCUMENT NUMBER: 127:210381
TITLE: Prolonged preservation of blood platelets and prevention of cytokine generation by platelets using

inhibitor compositions and cold temperatures
INVENTOR(S): Livesey, Stephen A.; Conner, Jerome; Currie, Laura M.
PATENT ASSIGNEE(S): Lifecell Corporation, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9730350 | A1 | 19970821 | WO 1997-US2365 | 19970213 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 6221669 | B1 | 20010424 | US 1996-600343 | 19960213 |
| AU 9722739 | A1 | 19970902 | AU 1997-22739 | 19970213 |
| EP 880695 | A1 | 19981202 | EP 1997-905974 | 19970213 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |

PRIORITY APPLN. INFO.: US 1996-600343 A 19960213
US 1994-326036 A2 19941019
WO 1997-US2365 W 19970213

AB This invention provides a method for prolonging the preservation of human blood platelets at reduced temps. The method uses an inhibitor system that enables blood platelets to retain their functional integrity during storage. In addn., the inhibitor system prevents the generation of cytokines in the platelet prepn. during storage at both 22.degree.C and 4.degree.C. This is accomplished by interrupting normal platelet function during storage, so as to help keep platelets from activating and losing their shape. Before using the platelets in a transfusion, they are returned to their normal functional level by washing the inhibitor system away from the platelets. This general method is exemplified using a soln. of inhibitors including amiloride, ticlopidine, dipyridamole, sodium nitroprusside, adenosine, and quinacrine. In all tests of viability and functional activity, the platelet conc. stored at 4.degree.C with the addn. of the inhibitor system of this invention displayed higher recovery at day 10 than the conventionally stored platelets at day 5. For all of the cytokines tested, the inhibitor-treated platelet prepns. produced lower amts. of cytokines during storage regardless of the incubation temp. of the cells.

IC ICM G01N031-00
ICS A01N001-02
CC 63-6 (Pharmaceuticals)
IT **Membrane**, biological
(modifier; prolonged preservation of blood platelets and prevention of cytokine generation by platelets using inhibitor compns. and cold temps.)
IT 9013-93-8, **Phospholipase** 9029-60-1, Lipoxygenase 39391-18-9, Cyclooxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(pathway inhibitor; prolonged preservation of blood platelets and prevention of cytokine generation by platelets using inhibitor compns. and cold temps.)

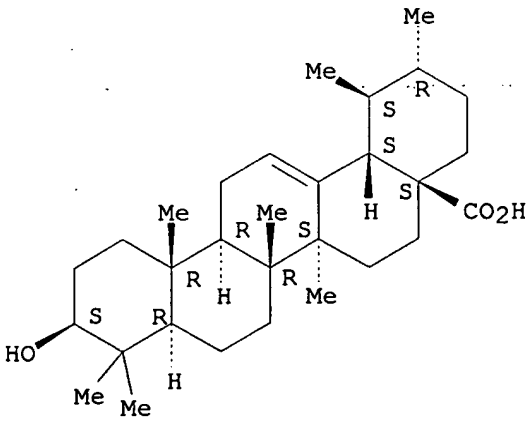
IT 50-56-6, Oxytocin, biological studies 50-78-2, Aspirin 53-86-1, Indomethacin 55-63-0, Glyceryl trinitrate 57-96-5, Sulfinpyrazone 58-32-2, Dipyridamole 58-55-9, Theophylline, biological studies 58-61-7, Adenosine, biological studies 74-79-3, L-Arginine, biological studies **77-52-1, Ursolic acid** 83-89-6, Quinacrine 93-35-6, Umbelliferone 123-31-9, Benzohydroquinone, biological studies 305-01-1, Esculetin 362-74-3, DBcAMP 363-24-6, PGE2 768-94-5, Amantadine 1191-85-1, 5,8,11,14-Eicosatetraynoic acid 2609-46-3, Amiloride 2609-46-3D, Amiloride, analogs 2898-76-2, Benzamil 5051-62-7, Guanabenz 5104-49-4, Flurbiprofen 6493-05-6, Pentoxifylline 7683-59-2, Isoproterenol 9002-71-5, Thyrotropin 10024-97-2, Nitrous oxide, biological studies 11000-17-2, Vasopressin 14402-89-2, Sodium nitroprusside 15687-27-1, Ibuprofen 22071-15-4, Ketoprofen 23583-48-4, 8-Bromo cAMP 26687-79-6, SIN-1A 28822-58-4, Isobutylmethyl xanthine 33876-97-0, SIN-1 34031-32-8, Auranofin 35080-11-6, Prajmalium 35121-78-9, Prostacyclin 35523-89-8, Saxitoxin 37205-61-1, Proteinase inhibitor 54143-55-4, Flecainide 55142-85-3, Ticlopidine 64706-54-3, Bepridil 66575-29-9, Forskolin 78919-13-8, Iloprost 85637-73-6, Atrial natriuretic factor 92285-01-3, Ajoene
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prolonged preservation of blood platelets and prevention of cytokine generation by platelets using inhibitor compns. and cold temps.)

IT **77-52-1, Ursolic acid**
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prolonged preservation of blood platelets and prevention of cytokine generation by platelets using inhibitor compns. and cold temps.)

RN 77-52-1 HCAPLUS

CN Urs-12-en-28-oic acid, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



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=> d que
L7            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "URSOLIC ACID"/CN
L8            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "RETINOIC ACID"/CN
L9         1767 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7
L19        1074 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CERAMIDE(3A)(FAT? OR LIPID?)
L20           0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L9 OR URSOLIC ACID) AND L19
L21          11 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L9 OR URSOLIC ACID) AND
                 (FREE(5A)FATTY ACID)
L22           8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L8 OR RETINOIC ACID) AND L19

L27           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L8 OR RETINOIC ACID) AND
                 FREE(5A)FATTY ACID(10A)(INCREAS? OR BOOST? OR ENHANC? OR
                 EXPAND? OR RAIS? OR STEP UP)
L28           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  STEROID(10A)(CERAMID?(5A)(LIPI
                 D? OR FAT?))
L30           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  STEROID (10A) FREE(5A)FATTY
                 ACID(10A)(INCREAS? OR BOOST? OR ENHANC? OR EXPAND? OR RAIS? OR
                 STEP UP)
L31          27 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 OR L21 OR L22 OR L27 OR
                 L28 OR L30

=> d ibib abs hitind l31 1-27

L31  ANSWER 1 OF 27  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:        2003:631128  HCAPLUS
TITLE:                   Effect of retinoids and borage seed oil on stratum
                         corneum lipid organization
AUTHOR(S):               Ramakrishnan, Srividya; Moore, David
CORPORATE SOURCE:        Unilever Research, Edgewater, NJ, 07020, USA
SOURCE:                  Abstracts of Papers, 226th ACS National Meeting, New
                         York, NY, United States, September 7-11, 2003 (2003),
                         COLL-325. American Chemical Society: Washington, D.
                         C.
                         CODEN: 69EKY9
DOCUMENT TYPE:           Conference; Meeting Abstract
LANGUAGE:                English
AB   Retinoids are important actives for dermatol. conditions, and are
     formulated into skin care products that are applied topically on skin.
     The objective of this work was to understand the effect of retinol and
     retinoic acid, and anti-irritants such as borage seed
     oil on the organization of corneum lipids. A model lipid barrier,
     consisting of the major constituents of corneum lipids -
     ceramides, cholesterol and fatty acids (per-deuterated
     stearic acid) - was used to study the effect of retinoids with FTIR and
     DSC. The CD2 scissoring mode of stearic acid methylenes, and CH2 rocking
     mode of ceramide methylenes, were each split into two components,
     indicating that they both exist as sep. phases with orthorhombic packing,
     with the ceramides remaining ordered up to higher temps. This behavior
     has been previously obsd. The addn. of retinol at concns. as low as 1%
     (1.5mol%) caused disordering of the lipid bilayers, as evidenced by the
     lower lipid disordering temp. from the CH2 and CD2 stretching frequency
     and DSC melting peaks, and disappearance of the CD2 and CH2 splitting at
     lower temps. This effect is more pronounced with 10% retinol.
     Interestingly, stratum corneum that had been treated with retinol in an
     oil recovered the original lipid melting transition when treated with
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borage seed oil. The mechanism for this recovery, and the effect of **retinoic acid** is currently being investigated.

L31 ANSWER 2 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:952726 HCAPLUS
DOCUMENT NUMBER: 138:395628
TITLE: Ceramide Signaling in Fenretinide-Induced Endothelial Cell Apoptosis
AUTHOR(S): Erdreich-Epstein, Anat; Tran, Linda B.; Bowman, Nina N.; Wang, Hongtao; Cabot, Myles C.; Durden, Donald L.; Vlckova, Jitka; Reynolds, C. Patrick; Stins, Monique F.; Groshen, Susan; Millard, Melissa
CORPORATE SOURCE: Keck School of Medicine, Department of Pediatrics, Childrens Hospital Los Angeles, Division of Hematology-Oncology, University of Southern California, Los Angeles, CA, 90027, USA
SOURCE: Journal of Biological Chemistry (2002), 277(51), 49531-49537
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Stress stimuli can mediate apoptosis by generation of the **lipid** second messenger, **ceramide**. Herein we investigate the mol. mechanism of ceramide signaling in endothelial apoptosis induced by fenretinide (N-(4-hydroxyphenyl)retinamide (4-HPR)). 4-HPR, a synthetic deriv. of **retinoic acid** that induces ceramide in tumor cell lines, has been shown to have antiangiogenic effects, but the mol. mechanism of these is largely unknown. We report that 4-HPR was cytotoxic to endothelial cells (50% cytotoxicity at 2.4 .mu.M, 90% at 5.36 .mu.M) and induced a caspase-dependent endothelial apoptosis. 4-HPR (5 .mu.M) increased ceramide levels in endothelial cells 5.3-fold, and the increase in ceramide was required to achieve the apoptotic effect of 4-HPR. The 4-HPR-induced increase in ceramide was suppressed by inhibitors of ceramide synthesis, fumonisin B1, myriocin, and L-cycloserine, and 4-HPR transiently activated serine palmitoyltransferase, demonstrating that 4-HPR induced de novo ceramide synthesis. Sphingomyelin levels were not altered by 4-HPR, and desipramine had no effect on ceramide level, suggesting that sphingomyelinase did not contribute to the 4-HPR-induced ceramide increase. Finally, the pancaspase inhibitor, t-butyloxycarbonyl-aspartyl[O-methyl]-fluoromethyl ketone, suppressed 4-HPR-mediated apoptosis but not ceramide accumulation, suggesting that ceramide is upstream of caspases. Our results provide the first evidence that increased ceramide biosynthesis is required for 4-HPR-induced endothelial apoptosis and present a mol. mechanism for its antiangiogenic effects.
CC 1-6 (Pharmacology)
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:617104 HCAPLUS
DOCUMENT NUMBER: 136:319314
TITLE: Lipid analysis of follicular casts from cyanoacrylate strips as a new method for studying therapeutic effects of antiacne agents

AUTHOR(S): Thielitz, A.; Helmdach, M.; Ropke, E-M.; Gollnick, H.
CORPORATE SOURCE: Department of Dermatology and Venereology, Medical Faculty, Otto Von Guericke University Magdeburg, Magdeburg, D-39120, Germany
SOURCE: British Journal of Dermatology (2001), 145(1), 19-27
CODEN: BJDEAZ; ISSN: 0007-0963
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The cyanoacrylate follicular biopsy is an established method for the examn. of the horny layer and quant. assessment of microcomedones. We have optimized the method by sepg. follicular casts mech. from the cyanoacrylate strips. To use this method to analyze topical therapy-induced changes of the lipid compn. in the sebaceous follicular infundibulum. Both the follicular casts and the residual skin surface strip, the last representing a mixt. of stratum corneum and surface lipids, were extd. twice with n-hexane-ethanol under ultrasonication, evapd., redissolved in chloroform-methanol and sepd. by high-performance thin layer chromatog., using cholesterol sulfate, cerebroside, ceramide types 3 and 4, cholesterol, oleic acid, triolein, cholesterol oleate and squalene as stds. Identification was performed by computer-assisted densitometric anal. Six patient groups receiving adapalene 0.1%, tretinoin 0.025%, clindamycin 1%, clindamycin 1% + tretinoin 0.025%, benzoyl peroxide 5% or benzoyl peroxide 5% + erythromycin 2% were investigated before and 12 wk after application. A significant decrease in **free fatty acid** proportions combined with an **increase** in triglycerides was obsd. in the groups receiving antimicrobial therapy, supporting the hypothesis of lipolysis due to microbial colonization. The groups treated with topical retinoids showed an addnl. significant increase in ceramide subfractions, most probably reflecting their influence on epidermal keratinization. Our method proved suitable for the detection of quant. and qual. changes in lipid profiles of both infundibulum cast content and surface lipids. It enabled simple, non-invasive and objective assessment of the most relevant lipid classes in the sebaceous infundibulum, and efficient monitoring of drug effects on the follicular infundibulum.

CC 1-12 (Pharmacology)
Section cross-reference(s): 63

IT **Ceramides**
Cerebrosides
Fatty acids, biological studies
Glycerides, biological studies
Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**lipid** anal. of follicular casts from cyanoacrylate strips as a new method for studying therapeutic effects of antiacne agents)

IT 94-36-0, Benzoyl peroxide, biological studies 114-07-8, Erythromycin **302-79-4**, Tretinoin 18323-44-9, Clindamycin 106685-40-9, Adapalene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid anal. of follicular casts from cyanoacrylate strips as a new method for studying therapeutic effects of antiacne agents)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:165835 HCAPLUS
DOCUMENT NUMBER: 134:198119
TITLE: Methods for potentiation of efficacy of topical actives by monoacyl-(lyso)-glycerophosholipids
INVENTOR(S): Bishop, Michael; Gillis, Glen; Norton, Scott J.
PATENT ASSIGNEE(S): Active Organics Inc., USA
SOURCE: Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 1080719 | A2 | 20010307 | EP 2000-118980 | 20000901 |
| EP 1080719 | A3 | 20010425 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002128702 | A2 | 20020509 | JP 2001-262591 | 20010831 |

PRIORITY APPLN. INFO.: US 1999-152305P P 19990903
US 2000-654421 A 20000901

AB Mono-acyl-(lyso)-glycerophospholipids (also known as lysophosphatidyl derivs.; e.g., lysophosphatidylcholine, lysolecithin, lysophosphatidylserine, lysocephalin), are used either alone or in combination with certain other permeation-enhancing compds., to enhance the penetration of active ingredients into the vertebrate epidermis and thus enhance and/or potentiate the efficacy of topically-applied active components. Other permeation-enhancing compds. which may be included in formulations with mono-acyl-(lyso)-glycerophospholipids include, but are not limited to, salicylates, esters of choline, acyl carnitines, diethoxyglycol, and detergents such as sodium dodecyl sulfate, lecithins and other phosphatidyl compds., and other surface-active **lipid** derivs., such as **ceramides** and cerebrosides. A topical gel contained monoacyl glycerolysophospholipids 0.3, butylene glycol 10, K sorbate 0.07, Natrasol 250HHR 2, citric acid 3, NaOH 0.45, retinol palmitate 0.3, and distd. water q.s. to 100 %.

IC ICM A61K009-70
ICS A61K047-24

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 62

IT 55-92-5, Methacholin 57-83-0, Progesterone, biological studies 58-22-0, Testosterone 73-31-4, Melatonin 79-81-2, Retinol palmitate **302-79-4, Retinoic acid** 9002-79-3, MSH 61912-98-9, IGF
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glycerolysophospholipids for percutaneous enhancement of actives)

L31 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:129315 HCAPLUS
DOCUMENT NUMBER: 134:364149
TITLE: Developmental changes of cuticular constituents and their association with ethylene during fruit ripening in 'Delicious' apples
AUTHOR(S): Ju, Z.; Bramlage, W. J.
CORPORATE SOURCE: Department of Plant and Soil Sciences, University of

Massachusetts, Amherst, MA, 01003, USA
SOURCE: Postharvest Biology and Technology (2001), 21(3), 257-263
CODEN: PBTEED; ISSN: 0925-5214
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Developmental changes in total cuticle and cuticular constituents and their responses to ethylene during fruit ripening were studied using 'Delicious' apples. Total chloroform extractable wax and total cutin (including carbohydrate polymers) were 3.1 and 5.4 g m-2, resp., in young fruit. They increased during fruit development and reached 14.1 and 24.7 g m-2 of fruit peel, resp., at harvest. During postharvest fruit ripening at 20.degree.C, total cutin did not change but total wax increased to 21.5 g m-2 at 6 wk. The increase of cuticular wax paralleled the increase of internal ethylene in fruit. Wax was sepd. by column chromatog. into four portions - hydrocarbons and wax esters, **free** alcs., **free fatty acids**, and diols. More than half of the diol fraction was **ursolic acid**. During fruit development, more hydrocarbons and diols than **free fatty acids** and alcs. accumulated in cuticle. During fruit ripening, all four portions increased, coinciding with the climacteric rise in ethylene, but rates of increase of **free fatty acids** and alcs. were higher than those of other portions. Preharvest treatment with 220 mg l-1 aminoethoxyvinylglycine (AVG) inhibited internal ethylene to <0.5 mg l-1 during 6 wk at 20.degree.C and no wax accumulation was detected in AVG-treated fruit. Preharvest treatment with 200 mg l-1 ethephon increased internal ethylene and accelerated wax accumulation compared with controls. Ethephon accelerated and AVG inhibited .alpha.-farnesene accumulation.
CC 11-3 (Plant Biochemistry)
IT **77-52-1, Ursolic acid** 502-61-4, .alpha.-Farnesene 54990-88-4, Cutin
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(developmental changes of cuticular constituents assocd. with ethylene during fruit ripening of 'Delicious' apples)
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:158232 HCAPLUS
DOCUMENT NUMBER: 132:288111
TITLE: Enhancement of fluorescence in thin-layer chromatography induced by the interaction between n-alkanes and an organic cation
AUTHOR(S): Cossio, Fernando P.; Arrieta, Ana; Cebolla, Vicente L.; Membrado, Luis; Domingo, Maria P.; Henrion, Patrick; Vela, Jesus
CORPORATE SOURCE: Kimika Fakultatea, Euskal Herriko Unibertsitatea, San Sebastian-Donostia, 20080, Spain
SOURCE: Analytical Chemistry (2000), 72(8), 1759-1766
CODEN: ANCHAM; ISSN: 0003-2700
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Fluorescence enhancement of a broad variety of solutes was used

extensively in TLC although no thorough explanation is proposed. The authors try to understand it and explore new applications to which it can be put. In this way, alkanes can be quant. detd. by fluorescence scanning densitometry using silica gel plates impregnated with berberine sulfate. Mol. simulation and anal. of MOs allows this phenomenon to be explained in this case and lays the groundwork to explain fluorescence enhancements produced by other mols. A ion-mol. interaction between alkanes and berberine sulfate is responsible for the enhancement of fluorescence produced by alkanes. Computational results suggest that the surrounding alkane mols. provide an apolar environment to the berberine cation, thus enhancing the intensity of the fluorescence signal. This proposed explanation was tested by extending the fluorescence detn. to other compds. These include biol. interesting satd. and unsatd. **fatty** acids, **steroids** and derivs., prostaglandins, **ceramides** , galactocerebrosides, as well as terpenes, and polypropylene glycols. According to the proposed explanation, the properties required for alternative impregnants to berberine are discussed.

CC 80-5 (Organic Analytical Chemistry)
Section cross-reference(s): 22, 26, 37, 51, 73

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 7 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:810383 HCAPLUS
DOCUMENT NUMBER: 132:103037
TITLE: Evaluation of model for stratum corneum lipid barrier against steroid diffusion
AUTHOR(S): Trotta, M.; Carlotti, M. E.; Gallarate, M.
CORPORATE SOURCE: Dipartimento di Scienza e Tecnologia del Farmaco, Turin, 10125, Italy
SOURCE: Journal of Dispersion Science and Technology (1999), 20(7), 1831-1847
CODEN: JDTEDS; ISSN: 0193-2691
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The ability of three matrixes to model the barrier properties of the lipid domain of stratum corneum (SC) against permeation of seven steroids was studied. Model matrixes were water and oleic acid/oleate; a mixt. of unsatd. and satd. fatty acids/soap; or a more complex matrix also contg. phospholipids, sphingolipids, cholesterol and ceramides. Permeability coeffs. (K) were similar in the three models, supporting the hypothesis that the barrier to steroid permeation is detd. by the structural organization of the lipids, not by the chem. structure of individual substances. Parabolic relationships were found between K values and octanol/water partition coeffs. (Poct) of the steroids, with an optimum permeability at log Poct of 3.0. All three models showed good resistance to permeability by steroids. The effects of cationic, anionic and non-ionic surfactants on the permeability of hydrocortisone within the water oleic acid/oleate matrix were also investigated. Permeability increased with anionic surfactants, decreased with cationic surfactants and varied little with non-ionic surfactants. The matrixes tested appeared able to model the effect of surfactants on the permeability of hydrocortisone through the SC.

CC 2-4 (Mammalian Hormones)

IT **Ceramides**
RL: BUU (Biological use, unclassified); DEV (Device component use); BIOL

(Biological study); USES (Uses)
(stratum corneum **lipid** barrier model evaluation for **steroid** permeation)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:307480 HCAPLUS
DOCUMENT NUMBER: 130:321012
TITLE: Effects of free fatty acids on free form fraction of steroids in human serum
AUTHOR(S): Watanabe, Sadao
CORPORATE SOURCE: Kanagawa Prefect. Public Health Lab., Yokohama, 241-0815, Japan
SOURCE: Journal of Health Science (1999), 45(2), 93-99
CODEN: JHSCFD
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Steroids are transported in free forms and also in bound forms with .beta.-globulin and/or with albumin in serum, and bind to with an intracellular specific 'receptor' protein after permeation through the cell membrane of target cell. Albumin and globulin cannot permeate through the cell membrane, so it has been generally assumed that the concn. of steroids in free forms dets. the uptake rate and its bioavailability. The effects of the addn. of such free fatty acids as palmitic acid, oleic acid, and linoleic acid to the fractions of free .beta.-estradiol and testosterone in serum were examd. in vitro. It was found that the concn. of free steroids did not vary at the normal levels (when the range of the molar ratios of free fatty acid/albumin in serum was from 0.5 to 2) in men and women, but when the molar ratios of **free fatty acid**/albumin exceeded 3 the concn. of free **steroids increased** by the addn. of **free fatty acids**. The effects of **free fatty acids** on the **increase** of the concn. of free **steroids** fraction were in the following order : linoleic acid, oleic acid > palmitic acid. These results suggest that the elevation of the concn. of free fatty acids in serum, amplified by high fat consumption, obesity and stress, may cause the increases of physiol. active .beta.-estradiol and testosterone.
CC 2-4 (Mammalian Hormones)

L31 ANSWER 9 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:582825 HCAPLUS
DOCUMENT NUMBER: 130:213
TITLE: Regulation of G1/S transition and induction of apoptosis in HL-60 leukemia cells by fenretinide (4HPR)
AUTHOR(S): DiPietrantonio, Anna M.; Hsieh, Tze-Chen; Olson, Susan C.; Wu, Joseph M.
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, New York Medical College, Valhalla, NY, 10595, USA
SOURCE: International Journal of Cancer (1998), 78(1), 53-61
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors previously reported that all-trans **retinoic acid** (RA) and fenretinide (4HPR) suppress HL-60 leukemia cell growth and cause partial cell arrest in the G1-to-S phase. Moreover, 4HPR but not RA induces apoptosis in HL-60 cells. To investigate further the obsd. biol. effects, cyclin D1 and cdk4 expression and the level of phosphorylation of the retinoblastoma protein Rb were assessed. Cyclin D1 and cdk4 expression and Rb phosphorylation were significantly reduced, by 40-75%, after 24 h of treatment with RA or 4HPR; these decreases were either transient, e.g., only at 24 h for cdk4, or sustained for 72 h. In general, more pronounced decreases were seen in the 4HPR-treated cells. Evidence for 4HPR-induced apoptosis comes from (1) cleavage of the enzyme poly(ADP-ribose) polymerase (PARP) to an 89-kDa truncated product, (2) appearance of DNA ladders on agarose gel electrophoresis, and (3) higher incorporation in situ of digoxigenin nucleotides into the free 3'-ends of DNA. Overnight pretreatment with 0.5-5.0 .mu.M of the CPP32 inhibitor DEVD, but not the ICE inhibitor YVAD, significantly reduced the specific processing of PARP, suggesting that CPP32 is involved in the mechanism of action of 4HPR. Anal. of 2 **lipid**-derived second messengers, **ceramide** and diacylglycerol (DAG), as a function of time of treatment with RA or 4HPR, showed ceramide but not DAG to be significantly albeit transiently increased 2-fold at 3 h, by 4HPR. To test further whether ceramide may be involved in the signaling cascade that culminates in the induction of apoptosis in 4HPR-treated HL-60 cells, the effects of fumonisin B1, an inhibitor of ceramide synthase, were studied. Simultaneous treatment of cells with 4HPR and 25-100 .mu.M fumonisin B1 resulted in a dose-dependent redn. in the elevation in ceramide, the extent of PARP cleavage, and induction of apoptosis. Pretreatment with DEVD or YVAD, had no effect on the 4HPR-induced increase in ceramide.

CC 1-6 (Pharmacology)

IT Cyclins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(D1; regulation of G1/S transition and induction of apoptosis in HL-60 leukemia cells by fenretinide in relation to biochem. mechanism and **retinoic acid**)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Rb, phosphorylation; regulation of G1/S transition and induction of apoptosis in HL-60 leukemia cells by fenretinide in relation to biochem. mechanism and **retinoic acid**)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(gene cdk4; regulation of G1/S transition and induction of apoptosis in HL-60 leukemia cells by fenretinide in relation to biochem. mechanism and **retinoic acid**)

IT Antitumor agents
(leukemia; regulation of G1/S transition and induction of apoptosis in HL-60 leukemia cells by fenretinide in relation to biochem. mechanism and **retinoic acid**)

IT Apoptosis
Second messenger system
(regulation of G1/S transition and induction of apoptosis in HL-60 leukemia cells by fenretinide in relation to biochem. mechanism and **retinoic acid**)

IT Ceramides

Diglycerides
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(regulation of G1/S transition and induction of apoptosis in HL-60 leukemia cells by fenretinide in relation to biochem. mechanism and **retinoic acid**)
IT **302-79-4**, all-trans-**Retinoic acid**
65646-68-6, Fenretinide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(regulation of G1/S transition and induction of apoptosis in HL-60 leukemia cells by fenretinide in relation to biochem. mechanism and **retinoic acid**)
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:268334 HCAPLUS
DOCUMENT NUMBER: 129:8587
TITLE: Method and compositions for disrupting the epithelial barrier function
INVENTOR(S): Elias, Peter M.; Feingold, Kenneth R.; Holleran, Walter M.; Thornfeldt, Carl R.
PATENT ASSIGNEE(S): Regents of the University of California, USA; Cellegy Pharmaceuticals, Inc.
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9817253 | A1 | 19980430 | WO 1997-US19343 | 19971022 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9749193 | A1 | 19980515 | AU 1997-49193 | 19971022 |
| US 6190894 | B1 | 20010220 | US 1998-58401 | 19980409 |
| US 6562606 | B1 | 20030513 | US 2000-608568 | 20000630 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1996-733712 | A | 19961023 |
| US 1993-33811 | B2 | 19930319 |
| US 1994-260559 | B2 | 19940616 |
| WO 1997-US19343 | W | 19971022 |
| US 1998-58401 | A1 | 19980409 |

AB Epithelial barrier function is disrupted in a host in need of topical administration of a physiol. active substance by applying to the epithelium a barrier-disrupting amt. of .gtoreq.1 agent selected from (1) inhibitors of synthesis of **ceramides**, acylceramides, glucosylceramides, sphingomyelins, **fatty** acids, or cholesterol;

(2) degrdn. enzymes for ceramides, acylceramides, glucosylceramides, or sphingomyelins; (3) inhibitors of degrdn. of phospholipids, glycosphingolipids, glucosylceramides, acylceramides, or sphingomyelins; and (4) inhibitors and stimulators of metabolic enzymes of free **fatty** acids, **ceramides**, and cholesterol. Thus, a combination of 5-tetradecyloxy-2-furancarboxylic acid (an inhibitor of acetyl-CoA carboxylase which is the rate-limiting enzyme in free fatty acid synthesis) and .beta.-chloroalanine (an inhibitor of serine palmitoyltransferase, the rate-limiting enzyme in ceramide synthesis) increased delivery of lidocaine through mouse stratum corneum by 8-fold in vivo and increased transepidermal water loss. Thus, a combination of 5-tetradecyloxy-2-furancarboxylic acid (an inhibitor of acetyl-CoA carboxylase which is the rate-limiting enzyme in free fatty acid synthesis) and .beta.-chloroalanine (an inhibitor of serine palmitoyltransferase, the rate-limiting enzyme in ceramide synthesis) increased delivery of lidocaine through mouse stratum corneum by 8-fold in vivo and increased transepidermal water loss.

IC ICM A61K009-10

CC 63-6 (Pharmaceuticals)

IT 50-02-2, Dexamethasone 50-24-8, Prednisolone 50-47-5, Desipramine 50-49-7, Imipramine 50-53-3, Chlorpromazine, biological studies 52-53-9, Verapamil 53-86-1, Indomethacin 54-05-7, Chloroquine 54-64-8, Thimerosal 57-55-6, Propylene glycol, biological studies 57-88-5D, Cholesterol, esters 67-42-5, EGTA 67-68-5, DMSO, biological studies 68-41-7, D-Cycloserine 78-41-1, Triparanol 83-89-6, Quinacrine 84-97-9D, Perazine, chloro derivs. 85-79-0, Dibucaine 92-84-2D, Phenothiazine, derivs. 98-80-6, Phenylboronic acid 99-73-0 111-58-0, N-Oleoylethanolamine 117-39-5, Quercetin 117-89-5, Trifluoperazine 118-42-3, Hydroxychloroquine 123-78-4D, Sphingosine, hexylglucosyl derivs. 137-58-6, Lidocaine 143-28-2, Oleyl alcohol 270-26-8, 7H-1,3-Dioxolo[4,5-h][3]benzazepine **302-79-4**, all-trans-**Retinoic acid** 303-43-5, Cholesterol oleate 313-05-3, 20,25-Diazacholesterol 339-72-0, L-Cycloserine 362-74-3, Dibutyryl cyclic AMP 366-93-8, AY 9944 390-64-7 481-49-2, Cepharanthine 525-66-6, Propranolol 526-87-4, Conduritol 872-50-4, N-Methylpyrrolidin-2-one, biological studies 1154-25-2 1256-86-6, Cholesterol sulfate 1393-88-0, Gramicidin D 1403-66-3, Gentamicin 1404-04-2, Neomycin 2001-96-9 2140-46-7, 25-Hydroxycholesterol 3821-81-6, .beta.-Fluoroalanine 3981-36-0, .beta.-Chloroalanine 4358-16-1, Cholesterol phosphate 4759-48-2, 13-cis-**Retinoic acid** 6090-95-5, Conduritol B-epoxide 6734-33-4 7287-36-7, Monalide 9034-40-6, LHRH 10238-27-4 10238-28-5 13095-61-9, 26-Hydroxycholesterol 13780-71-7, Boronic acid 19130-96-2, Deoxynojirimycin 21829-25-4, Nifedipine 22204-53-1, Naproxen 24579-86-0 24887-57-8, 22,25-Diazacholesterol 25265-75-2, Butanediol 25496-72-4, Glycerol monooleate 27848-84-6, Nicergoline 36894-69-6, Labetalol 42399-41-7, Diltiazem 54857-86-2, 5-Tetradecyloxy-2-furancarboxylic acid 55985-32-5, Nicardipine 57265-65-3, R-24571 58546-54-6, Gomisin A 59227-89-3, 1-Dodecylazacycloheptan-2-one 59865-13-3, Cyclosporin A 65595-90-6 66085-59-4, Nimodipine 67655-93-0, Esterastin 73573-88-3, Mevastatin 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 93957-55-2, Fluindostatin 96829-58-2, Tetrahydrolipstatin 116355-83-0, Fumonisin B1 117019-08-6 126661-83-4, Cyclophellitol 159440-05-8 159440-26-3 194038-29-4 207351-39-1 207351-40-4 207351-41-5 207351-42-6 207351-43-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method and compns. for disrupting the epithelial barrier function)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:547955 HCAPLUS
DOCUMENT NUMBER: 127:210181
TITLE: Effects of niacinamide on ceramide biosynthesis and differentiation of cultured human keratinocytes
AUTHOR(S): Tanno, Osamu; Ota, Yukiko; Mitamura, Nobuo; Inoue, Shintaro
CORPORATE SOURCE: Basic Res. Lab., Kanebo Ltd., Japan
SOURCE: Scientific Conference of the Asian Societies of Cosmetic Scientists, 3rd, Taipei, May 23-24, 1997 (1997), 170-176. Asian Societies of Cosmetic Scientists: Taichung, Taiwan.
CODEN: 64XSAZ
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Vitamins have been widely applied in skin care products, but the relationship between vitamin and stratum corneum lipid synthesis has not been well known. Stratum corneum **lipids**, particularly **ceramides**, are important components in epidermal permeability barrier. It has been reported that the level of ceramides is decreased in atopic dermatitis and aged skin. In this study, the effects of vitamins on sphingolipid biosyntheses including ceramides using cultured normal human keratinocytes were examd. The rate of sphingolipids biosyntheses was measured by the incorporation of 14C-serine into sphingolipids. When the cells were incubated with 1 to 10 .mu.M of niacinamide (NA) for 6 days, the rates of ceramide, cerebroside and sphingomyelin syntheses were increased dose-dependently up to 5-fold with 10 .mu.M compared with that of control. Other vitamins examd. showed no effects. Furthermore, the activity of serine-palmitoyl transferase, a rate-limiting enzyme in sphingolipid synthesis, was increased in NA-treated cells. These results indicate that NA stimulates de novo synthesis of sphingolipids in human keratinocytes. Because the morphol. changes of NA-treated cells were similar to those assocd. with the differentiation at a high Ca concn., the effect of NA on the differentiation of human keratinocytes at subconfluence was examd. Both cornified envelope formation and expression of a differentiated type keratin K1, were accelerated by NA treatment at the same range of concns. as above. Taken together, both the increase in sphingolipid biosynthesis and the enhancement of differentiation of keratinocyte cells were thought to accelerate the barrier recovery following the barrier perturbations. As an in vivo estn., the effect of NA on the permeability barrier perturbation in a murine model induced by all-trans **retinoic acid** (RA) was examd. When 0.01, 0.1 or 0.5% NA in 50% ethanol was applied topically to skin 6 h after RA application, the increase of transepidermal water loss assocd. with the degree of barrier disruption by RA was reduced in a dose dependent manner. These results indicate that topically applied NA prevents barrier disruption. In conclusion, our study demonstrates that NA is a useful vitamin to improve the permeability barrier integrity.

CC 62-4 (Essential Oils and Cosmetics)
Section cross-reference(s): 1, 63

L31 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:547161 HCAPLUS
DOCUMENT NUMBER: 125:291904
TITLE: Methodology, mechanism and application of charge-remote fragmentation in the gas phase
AUTHOR(S): Li, Zhili; Liu, Shuying
CORPORATE SOURCE: Changchun Inst. Appl. Chem., Chinese Acad. Scis., Changchun, 130022, Peop. Rep. China
SOURCE: Fenxi Huaxue (1996), 24(8), 967-973
CODEN: FHHHDT; ISSN: 0253-3820
PUBLISHER: Zhongguo Huaxuehui "Fenxi Huaxue" Bianji Weiyuanhui
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 62 refs. is given on the recent studies of charge-remote fragmentation in the gas phase, including the methods of charge localization, the mechanism of charge-remote fragmentation and the applications in a no. of classes of compds. such as **fatty** acids, **steroids**, prostaglandins, complex **lipids**, **ceramides**, surfactants, peptides and certain antibiotics.
CC 80-0 (Organic Analytical Chemistry)
Section cross-reference(s): 73

L31 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:380832 HCAPLUS
DOCUMENT NUMBER: 125:110249
TITLE: Epicuticular and intracellular lipids of leaves of Hippophae rhamnoides
AUTHOR(S): Goncharova, N. P.; Glushenkova, A. I.
CORPORATE SOURCE: Inst. Khim. Rastit. Veshchestv, AN RUz, Tashkent, Uzbekistan
SOURCE: Khimiya Prirodnykh Soedinenii (1995), (6), 790-798
CODEN: KPSUAR; ISSN: 0023-1150
PUBLISHER: Fan
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Epicuticular lipids of sea buckthorn (H. rhamnoides) consisted of higher aliph. esters; fatty acids and aliph. acids and cyclic triterpene acids were also present. Intracellular lipids consisted of esters of alcs. with **fatty acids**; the alcs. were also present **free** and as acetates. Hydrocarbons, triglycerides, **free fatty acids**, carotenoids, and triterpene aldehydes and acids were also present.
CC 11-1 (Plant Biochemistry)
IT 57-10-3, Palmitic acid, biological studies 57-11-4, Stearic acid, biological studies 60-33-3, Linoleic acid, biological studies **77-52-1, Ursolic acid** 83-46-5, .beta.-Sitosterol 112-80-1, Oleic acid, biological studies 373-49-9, Palmitoleic acid 463-40-1, Linolenic acid 474-40-8, Citrostadienol 508-02-1, Oleanolic acid 544-63-8, Myristic acid, biological studies 545-46-0, Uvaol 545-48-2, Erythrodiol 559-70-6, .beta.-Amyrin 593-49-7, Heptacosane 630-03-5, Nonacosane 630-04-6, Hentriacontane 638-95-9, .alpha.-Amyrin 863-76-3, .alpha.-Amyrin acetate 915-05-9, .beta.-Sitosterol acetate 1449-09-8, 24-Methylenecycloartanol 1616-93-9, .beta.-Amyrin acetate 7235-40-7, .beta.-Carotene 16844-71-6, Epifriedelanol 16910-32-0, Obtusifoliol
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(epicuticular and intracellular lipids of leaves of Hippophae rhamnoides)

L31 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:216799 HCAPLUS
DOCUMENT NUMBER: 122:1102
TITLE: Method and compositions for disrupting the epithelial barrier function
INVENTOR(S): Elias, Peter M.; Thornfeldt, Carl R.; Grayson, Stephen
PATENT ASSIGNEE(S): Cellegy Pharmaceuticals, Inc., USA; Regents of the University of California
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9421230 | A1 | 19940929 | WO 1994-US3030 | 19940321 |
| W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| IL 109037 | A1 | 19990126 | IL 1994-109037 | 19940318 |
| AU 9465894 | A1 | 19941011 | AU 1994-65894 | 19940321 |
| EP 764017 | A1 | 19970326 | EP 1994-913927 | 19940321 |
| R: BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, PT, SE | | | | |
| US 5723114 | A | 19980303 | US 1996-639212 | 19960426 |
| US 5885565 | A | 19990323 | US 1996-638302 | 19960426 |
| US 6010691 | A | 20000104 | US 1996-639191 | 19960426 |

PRIORITY APPLN. INFO.: US 1993-33807 19930319
WO 1994-US3030 19940321
US 1994-261343 19940616

AB This invention relates generally to a novel method for enhancing penetration of physiol. active substances for cutaneous or transdermal delivery through epithelium which comprises the stratum corneum/epidermis and keratinizing mucous membranes. More specifically, it relates to a method and compn. for disrupting the epithelial barrier function in a host by applying to the epithelium a barrier-disrupting amt. of at least one agent selected from the group consisting of an inhibitor of ceramide synthesis, an inhibitor of acylceramide synthesis, an inhibitor of glucosylceramide synthesis, an inhibitor of sphingomyelin synthesis, an inhibitor of fatty acid synthesis, an inhibitor of cholesterol synthesis, a degrdn. enzyme of ceramides, acylceramide, glucosylceramides, sphingomyelin, an inhibitor of phospholipid, glycosphingolipid, including glucosylceramide, acylceramide or sphingomyelin degrdn., and both inhibitors and stimulators of metabolic enzymes of free **fatty** acids, **ceramide**, and cholesterol.

IC ICM A61K009-10
CC 1-12 (Pharmacology)
Section cross-reference(s): 63
IT 50-02-2, Dexamethasone 50-24-8, Prednisolone 50-47-5, Desipramine 50-49-7, Imipramine 50-53-3, Chlorpromazine, biological studies 52-53-9, Verapamil 53-86-1, Indomethacin 54-05-7, Chloroquine

54-64-8, Thimerosal 57-88-5, Cholesterol, biological studies 58-38-8, Prochlorperazine 67-42-5, EGTA 68-41-7, D-Cycloserine 78-41-1, Triparanol 83-89-6, Quinacrine 84-16-2D, Hexestrol, Diaminoethoxy derivs. 85-79-0, Dibucaine 98-80-6, Phenylboronic acid 99-73-0 111-58-0, N-Oleoylethanolamine 117-39-5, Quercetin 117-89-5, Trifluoperazine 118-42-3, Hydroxychloroquine 123-78-4D, Sphingosine, N-Hexylglucosyl derivs. **302-79-4**, all-trans-**Retinoic acid** 313-05-3, 20,25-Diazacholesterol 339-72-0, L-Cycloserine 362-74-3, Dibutyryl-cAMP 366-93-8, AY9944 390-64-7, Prenylamine 481-49-2, Cepharanthine 525-66-6, Propranolol 526-87-4, Conduritol 1154-25-2 1256-86-6, Cholesterol sulfate 1403-66-3, Gentamicin 1404-04-2, Neomycin 2001-96-9 2140-46-7, 25-Hydroxycholesterol 3821-81-6, .beta.-Fluoroalanine 3981-36-0, .beta.-Chloroalanine 4358-16-1, Cholesterol phosphate 4759-48-2, 13-cis-**Retinoic acid** 6090-95-5, Conduritol-B-epoxide 6734-33-4 9001-62-1, Acid lipase 9029-62-3, Squalene epoxidase 9077-14-9, Squalene synthetase 10238-27-4 10238-28-5 13095-61-9, 26-Hydroxycholesterol 13780-71-7, Boronic acid 19130-96-2, Deoxynojirimycin 21829-25-4, Nifedipine 22204-53-1, Naproxen 24579-86-0 24887-57-8, 22,25-Diazacholesterol 27848-84-6, Nicergoline 36894-69-6, Labetalol 42399-41-7, Diltiazem 52019-77-9 54857-86-2, 5-Tetradecyloxy-2-furancarboxylic acid 58546-54-6, Gomisin A 59865-13-3, Cyclosporin A 66085-59-4, Nimodipine 67655-93-0, Esterastin 73573-88-3, Mevastatin 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 85305-87-9, Glucosylceramides 89560-01-0 93957-55-2, Fluindostatin 95013-41-5, Calmidazolium 96829-58-2, Tetrahydrolipstatin 117019-08-6 126661-83-4, Cyclophellitol 137300-80-2 159440-05-8 159440-26-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method and compns. for disrupting epithelial barrier function for skin drug transport)

L31 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:98170 HCAPLUS
DOCUMENT NUMBER: 118:98170
TITLE: Seasonal, ontogenetic and variety specific changes in the surface wax of apple leaves
AUTHOR(S): Hellmann, Monica; Stoesser, Rudolf
CORPORATE SOURCE: Inst. Obst-, Gemuese- Weinbau, Univ. Hohenheim, Stuttgart, D-7000/70, Germany
SOURCE: Angewandte Botanik (1992), 66(3-4), 109-14
CODEN: ANBTAJ; ISSN: 0066-1759
DOCUMENT TYPE: Journal
LANGUAGE: German
AB The compn. of the surface wax from apple leaves of the varieties Gloster, Mutsu, Alkmene and the scab-resistant variety Prima was analyzed during seasonal and ontogenetic development. On av. the apple leaves had 28 .mu.g wax/cm2 leaf surface. The wax consisted of .apprx.60% triterpenoids and 10% alkanes, esters and primary alcs., resp. Aldehydes, sterols, secondary alcs., ketones and **free fatty acids** constituted the remaining 10%. These specifications characterize the av. surface wax, but the amt. and compn. of the wax changed strongly during the season, the development of the leaves, and in between the varieties. The total wax content increased during the season. Leaves of the same age, that means young as well as old ones, had in August .apprx.40% more wax than in May. During the development of the leaves esp. the compn. of

the wax changed. The amts. of alkanes and esters declined .apprx.50% while the amts. of the other components increased. Comparison of the surface wax of different varieties showed that the total wax content of Prima was about one third higher than that of Matsu. Gloster and Alkmene lay in between. Also some variety-specific differences in the compn. of the wax were found.

CC 11-3 (Plant Biochemistry)

IT **77-52-1, Ursolic acid** 83-46-5D, .beta.-Sitosterol, esters 506-52-5, Hexacosanol 508-02-1, Oleanolic acid 593-49-7, Heptacosane 629-99-2, Pentacosane 630-03-5, Nonacosane 630-04-6, Hentriacontane 630-05-7, Tritriacontane 22725-63-9, Triacontanal 22725-64-0, Octacosanal 26627-85-0, Hexacosanal 57866-08-7, Tetracosanal 57878-00-9, Dotriacontanal 76651-61-1, Hexatriacontanal 132912-09-5, Tetratriacontanal
RL: BIOL (Biological study)
(of apple leaf waxes, seasonal variation in)

L31 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:417686 HCAPLUS
DOCUMENT NUMBER: 111:17686
TITLE: Effects of isotretinoin on lipid metabolism in the rat
AUTHOR(S): McMaster, J.; Rogers, M. Perenna; Sherratt, H. S. A.; Shuster, S.
CORPORATE SOURCE: Dep. Pharmacol. Sci., Univ. Newcastle upon Tyne, Newcastle upon Tyne, NE2 4HH, UK
SOURCE: Archives of Dermatological Research (1989), 281(2), 116-18
CODEN: ADREDL; ISSN: 0340-3696
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Feeding rats a diet contg. isotretinoin (13-cis-**retinoic acid**) at 45 mg/kg increased the total serum and very-low-d. lipoprotein (VLDL) triacylglycerol and cholesterol concns. after 3 days. Higher doses of isotretinoin (.ltoreq.450 mg/kg) did not increase triacylglycerol earlier. There was an increase in the protein of VLDL and a decrease of that of high-d. lipoproteins, with no change in protein or cholesterol of low-d. lipoprotein. Fatty acid (oleic acid) metab. by hepatocytes was unchanged by treatment with isotretinoin, but serum levels of **free fatty acids** were **increased**

CC 1-12 (Pharmacology)

L31 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1988:546329 HCAPLUS
DOCUMENT NUMBER: 109:146329
TITLE: Chemical composition of the epicuticular wax of Dasyphyllum excelsum (Compositae, Mutisieae)
AUTHOR(S): Rivas, Pilar I.; Heinzen, Horacio; Moyna, Patrick; Niemeyer, Hermann M.
CORPORATE SOURCE: Fac. Cienc., Univ. Chile, Santiago, Chile
SOURCE: Revista Latinoamericana de Quimica (1988), 19(1), 34-5
CODEN: RLAQA8; ISSN: 0370-5943
DOCUMENT TYPE: Journal
LANGUAGE: Spanish

AB The epicuticular wax of D. excelsum is comprised of (%): free alcs. (24.8), aldehydes (12.6), hydrocarbons (19.2), hydroxy acids (15.1), esters (6.8), and **free fatty acids** (6.0).

The main constituent of the alc. fractions (free and esterified) is lupeol. This is the first time that aldehydes have been found in the epicuticular wax of a Compositae species. Another novel result is the co-occurrence of triterpenes and aldehydes in the wax, which has been previously detected only in turnip and grape waxes.

CC 11-1 (Plant Biochemistry)

IT **77-52-1, Ursolic acid** 508-02-1 545-47-1, Lupeol 545-47-1D, esters
RL: BIOL (Biological study)
(of epicuticular wax, of Dasyphyllum excelsum)

L31 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1984:626915 HCAPLUS
DOCUMENT NUMBER: 101:226915
TITLE: Components of Rosa nisami fruits
AUTHOR(S): Kuliev, V. B.; Gusarova, N. V.
CORPORATE SOURCE: Nakhichevan. Nauchn. Tsentr, Nakhichevan, USSR
SOURCE: Khimiya Prirodnykh Soedinenii (1984), (4), 536
CODEN: KPSUAR; ISSN: 0023-1150
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB R. nisami Seed contained 5.8 dry wt.% fatty oil contg. 2.7% **free fatty acids**. The fruit pulp contained 5.9% lipids, 4.01 dry wt.% ascorbic acid, **ursolic acid**, 0.93% carboxylic acids (as citric acid; citric, malic, and tartaric), free glucose and fructose, 5 free amino acids (leucine, methionine, valine, tyrosine, and threonine), 21.3% of a water-sol. polysaccharide, and 4.6% pectins.

CC 11-1 (Plant Biochemistry)

IT 50-81-7, biological studies 50-99-7, biological studies 57-48-7, biological studies **77-52-1** 77-92-9, biological studies 87-69-4, biological studies 6915-15-7 9000-69-5
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(of Rosa nisami fruit)

L31 ANSWER 19 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1984:169092 HCAPLUS
DOCUMENT NUMBER: 100:169092
TITLE: Isolation of prostaglandin E2-like material from osteonecrosis induced by steroids and its prevention by kallikrein inhibitor, aprotinin. An experimental study in rabbits
AUTHOR(S): Surat, Adil
CORPORATE SOURCE: Med. Sch., Hacettepe Univ., Ankara, Turk.
SOURCE: Prostaglandins, Leukotrienes and Medicine (1984), 13(2), 159-67
CODEN: PLMEDD; ISSN: 0262-1746
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Prostaglandin E2 (PGE2) [363-24-6]-like activity was increased in osteonecrotic femoral heads caused by high doses of methylprednisolone [83-43-2] in rabbits. Serum levels of cholesterol [57-88-5], total lipids, and **free fatty acids** were **increased** in rabbits with **steroid**-induced osteonecrosis as compared with controls. The rabbits given aprotinin [9087-70-1] together with the steroid showed significant decreases in serum cholesterol and lipid levels coupled with a marked further increase in the

local PGE2-like activity. Radiol. and histopathol. measurements indicated that aprotinin inhibited the osteonecrotic changes induced by steroid treatment, an effect that was not assocd. with a redn. in PGE2 levels.
CC 2-9 (Mammalian Hormones)
Section cross-reference(s): 14

L31 ANSWER 20 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1984:3565 HCAPLUS
DOCUMENT NUMBER: 100:3565
TITLE: Lipids of some medicinal plants
AUTHOR(S): Gusakova, S. D.; Stepanenko, G. A.; Asilbekova, D. T.; Murdokhaev, Yu. M.
CORPORATE SOURCE: Inst. Khim. Rast. Veshchestv, Tashkent, USSR
SOURCE: Rastitel'nye Resursy (1983), 19(4), 444-55
CODEN: RRESA8; ISSN: 0033-9946
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Seeds and other organs of 15 medicinal plant species contained 10-22 and 0.6-7.4% fat, resp. In addn. to triacylglycerols and **free fatty acids**, the seeds of Calendula officinalis and Erysimum diffusum contained .alpha.-carotene, Rhaponticum carthamoides .beta.-carotene, Potentialla erecta and Lavandula officinalis wax esters, etc. The C. officinalis and R. carthamoides seeds may supply easily-polymg. oils.
CC 11-1 (Plant Biochemistry)
IT **77-52-1**
RL: BIOL (Biological study)
(of Potentialla erecta)

L31 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1981:117785 HCAPLUS
DOCUMENT NUMBER: 94:117785
TITLE: Composition of extracts from the coats and kernel of Nepeta pannonica and Lavandula vera seeds
AUTHOR(S): Stepanenko, G. A.; Gusakova, S. D.; Umarov, A. U.
CORPORATE SOURCE: Inst. Khim. Rast. Veshchestv, Tashkent, USSR
SOURCE: Khimiya Prirodnykh Soedinenii (1980), (5), 614-20
CODEN: KPSUAR; ISSN: 0023-1150
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB The basic lipid compn. of seed coat and kernel of N. pannonica was generally identical, and the ext. from seed coat of L. vera contained usolic acid and its acetate. **Free fatty acids** of N. pannonica kernels consisted among others of satd. C20-35 fatty acids. From oil of L. vera seeds dimethyladipic acid was isolated. Lipids of Nepeta seed coat and kernel were high in triacylglycerides. The triglyceride content of L. vera kernel was also high (97.7% of the ext.).
CC 11-1 (Plant Biochemistry)
IT **77-52-1** 7372-30-7
RL: BIOL (Biological study)
(of seed coat of Lavandula vera)

L31 ANSWER 22 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1980:116231 HCAPLUS
DOCUMENT NUMBER: 92:116231
TITLE: Composition and structure of chemical constituents of rose flower stamen (Rosa damascena Miller)

AUTHOR(S): Hadieva, P.; Stoyanova-Ivanova, B.; Butchvarova, Z.; Daskalov, R.
CORPORATE SOURCE: Dep. Chem., Univ. Sofia, Sofia, Bulg.
SOURCE: Rivista Italiana Essenze, Profumi, Piante Officinali, Aromatizzanti, Syndets, Saponi, Cosmetici, Aerosols (1979), 61(6), 283-6
CODEN: RIEADU; ISSN: 0391-4658
DOCUMENT TYPE: Journal
LANGUAGE: English
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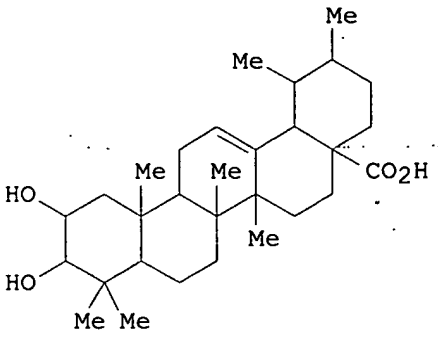


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AB The compn. of an ether ext. of Bulgarian rose stamen was studied for the first time. Tree triterpene components, new for the flowers of genus Rosa were isolated. They were 2-hydroxyursolic acid (I) [72881-13-1], .beta.-amyrin [559-70-6] and Me ursolate [32208-45-0], all of these known for their therapeutic action. The compn. of paraffins, olefins, .gamma.-diols, **free** and esterified with amyrin higher **fatty acids** was analyzed. The presence of the main rose oil monoterpene components was also established. The results are of importance in elucidating the various therapeutic actions of the medicines contg. Bulgarian rose oil or rose concrete.
CC 62-2 (Essential Oils and Cosmetics)
Section cross-reference(s): 63
ST rose flower stamen compn; **ursolic acid** rose stamen

L31 ANSWER 23 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1978:620786 HCAPLUS
DOCUMENT NUMBER: 89:220786
TITLE: Studies on the constituents of bezoar. Characterization of fatty acids and their cholesteryl esters
AUTHOR(S): Horii, Zenichi; Nagao, Keishiro; Kim, Sang-Won
CORPORATE SOURCE: Fac. Pharm. Sci., Josai Univ., Sakado, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1978), 26(5), 1607-10
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Various solvent extns. of Argentine bezoar (dried gallstone of the ox, Bos taurus domesticus) led to the isolation of cholesteryl esters of fatty acids, lithocholic acid, Me cholate, Me deoxycholate, Me

chenodeoxycholate, oleanolic acid, **ursolic acid**, and other (earlier reported) compds. Cholesteryl esters of **fatty acids** and **free fatty acids** were detd. by gas chromatog. and mass spectroscopy after converting them into Me esters by transesterification and diazomethane esterification, resp. The mixts. consisted essentially of C14-18 fatty acid esters with palmitate and stearate as the major components.

CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 13

IT 57-88-5D, esters with fatty acids **77-52-1** 434-13-9 508-02-1 3057-04-3 3245-38-3
RL: BIOL (Biological study)
(of Argentine bezoar)

L31 ANSWER 24 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1978:34925 HCAPLUS
DOCUMENT NUMBER: 88:34925
TITLE: Protein content and lipid constituents of the hoofs in horses
AUTHOR(S): Negishi, Takashi; Miyaki, Hideharu; Kameya, Tsutomu
CORPORATE SOURCE: Dep. Agro-Environ. Sci., Obihiro Univ. Agric. Vet. Med., Inada, Japan
SOURCE: Kyosoba Hoken Kenkyusho Hokoku (1977), 14, 22-8
CODEN: KHKHAS
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB The av. contents of N, lipids, and ash in the horse hoof were 16.5, 0.7, and 1.5%, resp. The N coeff. for the hoof proteins was 5.9, which was low as compared with other proteins. The hoof lipid consisted of 77-85% nonpolar and 15-23% polar lipids. The major nonpolar lipids were, in decreasing order: **steroid** esters, triglycerides, and **steroids**, and the major polar **lipid** was **ceramide** dihexoside. The major fatty acids of nonpolar lipids were palmitic, stearic, and oleic acids, whereas those of polar lipids were lignoceric, stearic, palmitic, and oleic acids. Thus, lipids must be taken into consideration for the protection of the equine hoof.

CC 13-1 (Mammalian Biochemistry)

L31 ANSWER 25 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1976:417119 HCAPLUS
DOCUMENT NUMBER: 85:17119
TITLE: Chemical constituents of the leaves of Callicarpa macrophylla Vahl
AUTHOR(S): Sengupta, Pasupati; Sen, Manju; Pal, Bikash C.; Pakrashi, Satyesh C.; Ali, Esahak
CORPORATE SOURCE: Org. Chem. Lab., Univ. Kalyani, Kalyani, India
SOURCE: Journal of the Indian Chemical Society (1976), 53(2), 218-19
CODEN: JICSAH; ISSN: 0019-4522
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An ext. of dried and powdered leaves of C. macrophylla was chromatographed over silica gel and eluted with Et2O-benzene (4:1). The Et ester of C23 **fatty acid**, **free** C22, C23, and C24 **fatty acids**, .beta.-sitosterol, .beta.-sitosterol-.beta.-D-glucoside, calliterpenone, calliterpenone monoacetate, **ursolic acid**, 2.alpha.-hydroxyursolic acid, and crategolic acid were

isolated and identified by m.p., NMR, and ir spectroscopy.
CC 11-1 (Plant Biochemistry)

L31 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1976:577 HCAPLUS
DOCUMENT NUMBER: 84:577
TITLE: Sex steroid influence on triglyceride metabolism
AUTHOR(S): Kim, Hak-Joong; Kalkhoff, Ronald K.
CORPORATE SOURCE: Div. Med., Med. Coll. Wisconsin, Milwaukee, WI, USA
SOURCE: Journal of Clinical Investigation (1975), 56(4), 888-96
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Triglyceride metab. was investigated in groups of fed and fasted rats after 21 days of parenteral estradiol benzoate (I) [50-50-0] (5 .mu.g daily), progesterone (II) [57-83-0] (5 mg daily), or the two steroids in combination. In rats given I sep. or combined with II, hypertriglyceridemia was uniformly assocd. with increased plasma triglyceride entry. II alone had no effect on these parameters. Plasma postheparin lipolytic activity (PHLA), adipose, mammary gland, and protamine-resistant lipoprotein lipase (LPL) [9004-02-8] were significantly increased in II-treated rats and significantly decreased in rats receiving I with the exception of mammary gland LPL, which was also increased to a slight extent. The combined regimen reduced plasma PHLA and increased protamine-resistant, adipose, and mammary gland LPL activity. Sex **steroid** treatments had minimal effects on plasma glucose and **free fatty acid** concns., but all **increased** plasma insulin [9004-10-8] significantly. Hyperinsulinemia did not parallel changes in body wt. or other measured parameters. Linear regression analyses revealed that plasma triglyceride concns. in all fed, treated rats correlated significantly with triglyceride entry but not very uniformly with plasma or tissue LPL activity. Apparently, I unlike II, has substantial lipemic effects in the rat which relate best to triglyceride entry. Hyperinsulinemia, changes in body wt., plasma PHLA, and tissue LPL activities did not consistently predict the influence of sex steroid treatment on plasma triglyceride concns.
CC 2-5 (Hormone Pharmacology)

L31 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1934:42538 HCAPLUS
DOCUMENT NUMBER: 28:42538
ORIGINAL REFERENCE NO.: 28:5147g-h
TITLE: Petroleum ether- and ether-soluble constituents of cranberry pomace
AUTHOR(S): Markley, K. S.; Sando, Charles E.
SOURCE: Journal of Biological Chemistry (1934), 105, 643-53
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The material examd. was air-dried cranberry pomace (waste) consisting of cuticle with some adhering cell tissue and seeds which made up about 25% of the wt. of the residue. The petroleum-ether ext. consisted of nonacosane and hentriacontane, **free** solid **fatty acids** of the series C16 to C26, oleic with smaller amts. of

linolenic and linoleic acids, a small amt. of glycerol probably originally in the form of fat, and small amts. of unidentified substances. The Et2O ext. (following extn. with petroleum ether) contained **ursolic acid** together with an unidentified resin acid.

CC 12 (Foods)

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=> d que
L7             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "URSOLIC ACID"/CN
L9          1767 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7
L10            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND (INCREAS?(5A)(LIPID?
                  OR FAT?))
L11            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND EPIDERM? AND KERAT?
L12         8184 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "SKIN (L) KERATINOCYTE"/CT
L13            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND (L12 OR KERATINOCYT?)
L14            7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 OR L11 OR L13

=> d ibib abs hitind hitstr l14 1-7

L14  ANSWER 1 OF 7  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2002:454831  HCAPLUS
DOCUMENT NUMBER:          138:192825
TITLE:                    Liposome-encapsulated ursolic acid increases ceramides
                          and collagen in human skin cells
AUTHOR(S):                Both, Dawn M.; Goodtzova, Karina; Yarosh, Daniel B.;
                          Brown, David A.
CORPORATE SOURCE:         AGI Dermatics, Freeport, NY, 11520, USA
SOURCE:                   Archives of Dermatological Research (2002), 293(11),
                          569-575
                          CODEN: ADREDL; ISSN: 0340-3696
PUBLISHER:                Springer-Verlag
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Skin wrinkling and xerosis assocd. with aging result from decreases in
     dermal collagen and stratum corneum ceramide content.  This study
     demonstrated that ursolic acid incorporated into liposomes (URA liposomes)
     increases both the ceramide content of cultured normal human
     epidermal keratinocytes (NHEK), and the collagen content
     of cultured normal human dermal fibroblasts.  In addn., URA liposomes
     increased the ceramide content of the skin of human subjects, with
     increases in hydroxy ceramides occurring after only 3 days of treatment.
     Both URA liposomes and retinoic acid decreased markers of
     keratinocyte differentiation (keratin 1, keratin
     10 and involucrin) in cultured NHEK.  Thus, URA liposomes have effects on
     keratinocyte differentiation and dermal fibroblast collagen
     synthesis similar to those of retinoids.  However, this study showed that
     URA liposomes increase ceramides in NHEK, in contrast to the decreases
     previously shown to be caused by retinoids.  URA liposomes have the
     potential to be used alone or in combination with other agents to restore
     or maintain skin ceramide and collagen content.
CC   62-4 (Essential Oils and Cosmetics)
IT   Keratins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (10; liposome-encapsulated ursolic acid increases ceramides and
        collagen in human skin cells)
IT   Keratins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (1; liposome-encapsulated ursolic acid increases ceramides and collagen
        in human skin cells)
IT   Skin
        (keratinocyte; liposome-encapsulated ursolic acid increases
        ceramides and collagen in human skin cells)
```
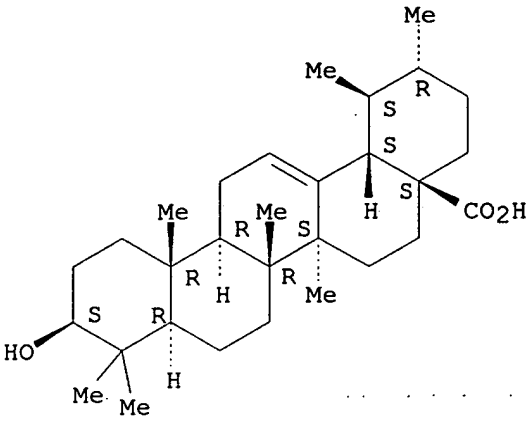

IT **77-52-1**, Ursolic acid
RL: BSU (Biological study, unclassified); COS (Cosmetic use); BIOL (Biological study); USES (Uses)
(liposome-encapsulated ursolic acid increases ceramides and collagen in human skin cells)
IT **77-52-1**, Ursolic acid
RL: BSU (Biological study, unclassified); COS (Cosmetic use); BIOL (Biological study); USES (Uses)
(liposome-encapsulated ursolic acid increases ceramides and collagen in human skin cells)
RN 77-52-1 HCAPLUS
CN Urs-12-en-28-oic acid, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).




REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:210687 HCAPLUS
DOCUMENT NUMBER: 137:103794
TITLE: Ursolic acid of Origanum majorana L. reduces A.beta.-induced oxidative injury
AUTHOR(S): Heo, Ho-Jin; Cho, Hong-Yon; Hong, Bumshik; Kim, Hye-Kyung; Heo, Tae-Ryeon; Kim, Eun-Ki; Kim, Sung-Koo; Kim, Chang-Ju; Shin, Dong-Hoon
CORPORATE SOURCE: Graduate School of Biotechnology, Korea University, Seoul, 136-701, S. Korea
SOURCE: Molecules and Cells (2002), 13(1), 5-11
CODEN: MOCEEK; ISSN: 1016-8478
PUBLISHER: Springer-Verlag Singapore Pte. Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Amyloid .beta. protein (A.beta.) **increases** free radical prodn. and **lipid** peroxidn. in PC12 nerve cells, leading to apoptosis and cell death. The effect of ursolic acid from Origanum majorana L. on A.beta.-induced neurotoxicity was investigated using PC12 cells. Pretreatment with isolated ursolic acid and vitamin E prevented the PC12 cell from reactive oxygen species (ROS) toxicity that is mediated by A.beta.. The ursolic acid resulted in decreased A.beta. toxicity assessed

by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), lactate dehydrogenase (LDH), and trypan blue assay. Thus, treatment with these antioxidants inhibited the A.beta.-induced neurotoxic effect. Therefore, these results indicate that micromolar A.beta.-induced oxidative cell death is reduced by ursolic acid from Origanum majorana L.

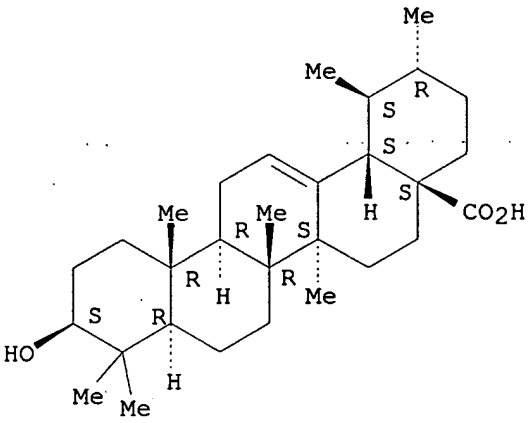
CC 1-11 (Pharmacology)
Section cross-reference(s): 11

IT **77-52-1P**, Ursolic acid
RL: PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ursolic acid of Origanum majorana L. reduces A.beta.-induced oxidative injury)

IT **77-52-1P**, Ursolic acid
RL: PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ursolic acid of Origanum majorana L. reduces A.beta.-induced oxidative injury)

RN 77-52-1 HCAPLUS
CN Urs-12-en-28-oic acid, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).




REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:31216 HCAPLUS
DOCUMENT NUMBER: 136:90707
TITLE: Skin conditioning compositions containing compounds for mimicking the effect of retinoic acid on skin
INVENTOR(S): Granger, Stewart Paton; Scott, Ian Richard; Donovan, Robert Mark; Iobst-Teklits, Susanne; Licameli, Lisa
PATENT ASSIGNEE(S): Unilever PLC, UK; Unilever NV; Hindustan Lever Limited
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002002074 | A2 | 20020110 | WO 2001-EP7234 | 20010625 |
| WO 2002002074 | A3 | 20030612 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| EP 1333800 | A2 | 20030813 | EP 2001-957886 | 20010625 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 2000-215301P P 20000630
WO 2001-EP7234 W 20010625

AB A skin care product comprising about 0.001-10% of a retinoid, in combination with at least two retinoid boosters (0.0001-50%). Retinoid boosters are selected from fatty acid amides, carotenoids, flavonoids, non-cyclic fragrance compds., phospholipid analogs, ureas, phosphatidylcholines, phosphatidylethanolamines, sphingomyelins, fatty acids, linseed oil, elaidic acid, bifonazole, climbazole, clotrimazole, econazole, quercetin, coumarin, quinolines, isoquinolines, etc. A compn. according to the invention is intended primarily as a product for topical application to human skin, esp. as an agent for conditioning and smoothening the skin, and preventing or reducing the appearance of wrinkled or aged skin. In use, a small quantity of the compn. is applied to exposed areas of the skin, from a suitable container or applicator and, if necessary, it is then spread over and/or rubbed into the skin using the hand or fingers or a suitable device. For example, a synergistic inhibition of transglutaminase, as a marker of skin differentiation, was obsd. by retinol with various quaternary combinations of retinoid boosters, e.g., acetyl sphingosine, phosphatidylcholine, linoleic acid, and climbazole.

IC ICM A61K007-48

CC 62-4 (Essential Oils and Cosmetics)

IT **Skin**
(**keratinocyte**, differentiation; skin conditioning compns. contg. retinoids and compds. mimicking effect of retinoic acid)

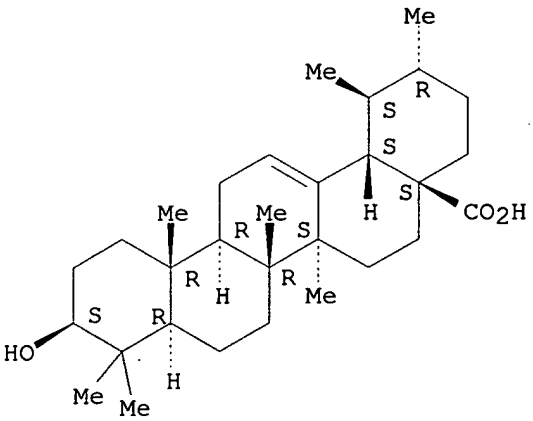
IT 54-36-4, Metyrapone 57-13-6D, Urea, derivs. 59-31-4, Carbostyril 60-33-3, Linoleic Acid, biological studies **77-52-1**, Ursolic acid 78-70-6, Linalool 79-78-7, Allyl .alpha.-ionone 80-73-9 91-22-5D, Quinoline, derivs. 91-64-5, Coumarin 97-78-9, Lauroyl sarcosine 98-55-5, .alpha.-Terpineol 106-14-9, 12-Hydroxystearic acid 106-22-9, Citronellol 106-24-1, Geraniol 112-79-8, Elaidic acid 117-39-5, Quercetin 119-65-3D, Isoquinoline, derivs. 121-33-5, Vanillin 127-41-3, .alpha.-Ionone 137-58-6, Lidocaine 141-10-6, Pseudoionone 141-43-5D, Ethanolamine, reaction products with castor oil or coco acyl derivs. 463-40-1, Linolenic Acid 471-53-4, Glycyrrhetinic Acid 480-41-1, Naringenin 505-54-4, Hexadecanedioic acid 506-32-1, Arachidonic acid 544-31-0 544-63-8, Myristic Acid, biological studies 553-03-7, Hydrocarbostyril 593-81-7D, Trimethylammonium chloride, coco derivs. 628-02-4, Hexanamide 629-22-1, 2-Hydroxystearic acid

695-10-3D, coco derivs. 871-37-4, Oleyl betaine 1632-73-1, Fenchyl alcohol 3102-57-6, N-Acetyl sphingosine 4602-84-0, Farnesol 5392-40-5, Citral 5697-56-3, Carbenoxolone 6540-56-3 7388-22-9, .gamma.-Methyl ionone 14417-88-0, Melinamide 16058-17-6 21145-77-7, Tonalid 22916-47-8, Miconazole 23593-75-1, Clotrimazole 23726-91-2, .beta.-Damascone 23726-93-4, Damascenone 23749-58-8 24034-73-9 27220-47-9, Econazole 27876-94-4, Crocetin 30399-84-9, Isostearic acid 30551-17-8, Nonadienal 31499-72-6, Dihydro-.alpha.-ionone 36574-66-0D, N-coco acyl derivs. 38083-17-9, Climbazole 39236-46-9, Imidazolidinyl urea 39799-78-5 43052-87-5, .alpha.-Damascone 51023-21-3, Oleyl hydroxyethylimidazoline 51264-14-3, Amsacrine 52558-73-3, N-Myristoyl sarcosine 54301-15-4, Amsacrine hydrochloride 56863-02-6, Linoleic diethanolamide 57378-68-4, .delta.-Damascone 59300-51-5, Santalone 60628-96-8, Bifonazole 61711-48-6, Isodamascone 65277-42-1, Ketoconazole 68171-52-8 68527-77-5, Isocyclogeraniol 68857-95-4, Traseolide 70788-30-6, Timberol 72089-08-8, Brahmanol 80449-46-3, Santanol 81613-56-1 93302-56-8, .alpha.-Methyl ionone 96760-44-0 112708-19-7, 1H-Benzotriazolamine 124753-97-5, N-Hexanoyl sphingosine 130066-44-3, Lyral 205579-27-7 386242-47-3 386242-62-2 386704-03-6, Utrecht 1 386704-13-8, Utrecht 2
RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
(skin conditioning compns. contg. retinoids and compds. mimicking effect of retinoic acid)

IT **77-52-1**, Ursolic acid
RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
(skin conditioning compns. contg. retinoids and compds. mimicking effect of retinoic acid)

RN 77-52-1 HCAPLUS
CN Urs-12-en-28-oic acid, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).




L14 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:743561 HCAPLUS
DOCUMENT NUMBER: 137:68038
TITLE: Liposomal Ursolic Acid (Merotaine) Increases Ceramides and Collagen in Human Skin
AUTHOR(S): Yarosh, Daniel B.; Both, Dawn; Brown, David
CORPORATE SOURCE: AGI Dermatics, Freeport, NY, USA

SOURCE: Hormone Research (2001), Volume Date 2000, 54(5-6), 318-321
CODEN: HRMRA3; ISSN: 0301-0163
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Skin wrinkling and xerosis assocd. with aging result from decreases of dermal collagen and stratum corneum ceramide content. This study demonstrates that ursolic acid incorporated into liposomes (Merotaine) increases both the ceramide content of cultured normal human **epidermal keratinocytes** and the collagen content of cultured normal human dermal fibroblasts. In clin. tests, Merotaine increased the ceramide content in human skin over an 11-day period. Merotaine has effects on **keratinocyte** differentiation and dermal fibroblast collagen synthesis similar to retinoids. However, unlike retinoids, Merotaine increases ceramide content of human **keratinocytes**. Ursolic acid may bind to members of the glucocorticoid receptor family to initiate changes in **keratinocyte** gene transcription.

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 13

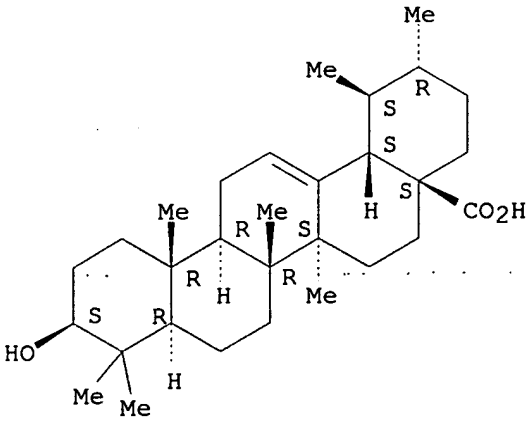
IT **Skin**
(**keratinocyte**; liposomal ursolic acid (Merotaine) increase of ceramides and collagen in human skin)

IT **77-52-1**, Ursolic acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Merotaine; liposomal ursolic acid (Merotaine) increase of ceramides and collagen in human skin)

IT **77-52-1**, Ursolic acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Merotaine; liposomal ursolic acid (Merotaine) increase of ceramides and collagen in human skin)

RN 77-52-1 HCAPLUS
CN Urs-12-en-28-oic acid, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).




REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS

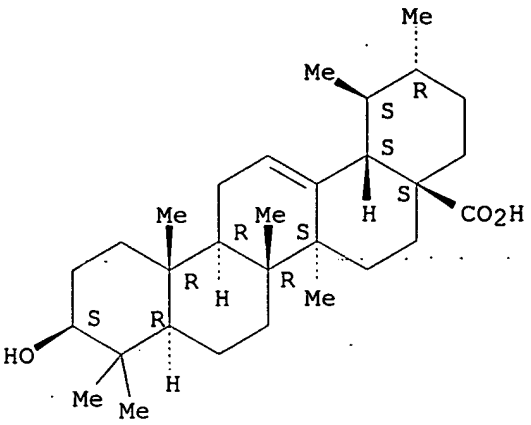
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:129315 HCAPLUS
DOCUMENT NUMBER: 134:364149
TITLE: Developmental changes of cuticular constituents and their association with ethylene during fruit ripening in 'Delicious' apples
AUTHOR(S): Ju, Z.; Bramlage, W. J.
CORPORATE SOURCE: Department of Plant and Soil Sciences, University of Massachusetts, Amherst, MA, 01003, USA
SOURCE: Postharvest Biology and Technology (2001), 21(3), 257-263
CODEN: PBTEED; ISSN: 0925-5214
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Developmental changes in total cuticle and cuticular constituents and their responses to ethylene during fruit ripening were studied using 'Delicious' apples. Total chloroform extractable wax and total cutin (including carbohydrate polymers) were 3.1 and 5.4 g m-2, resp., in young fruit. They increased during fruit development and reached 14.1 and 24.7 g m-2 of fruit peel, resp., at harvest. During postharvest fruit ripening at 20.degree.C, total cutin did not change but total wax increased to 21.5 g m-2 at 6 wk. The increase of cuticular wax paralleled the increase of internal ethylene in fruit. Wax was sepd. by column chromatog. into four portions - hydrocarbons and wax esters, free alcs., free fatty acids, and diols. More than half of the diol fraction was ursolic acid. During fruit development, more hydrocarbons and diols than free fatty acids and alcs. accumulated in cuticle. During fruit ripening, all four portions increased, coinciding with the climacteric rise in ethylene, but rates of **increase** of free **fatty** acids and alcs. were higher than those of other portions. Preharvest treatment with 220 mg l-1 aminoethoxyvinylglycine (AVG) inhibited internal ethylene to <0.5 mg l-1 during 6 wk at 20.degree.C and no wax accumulation was detected in AVG-treated fruit. Preharvest treatment with 200 mg l-1 ethephon increased internal ethylene and accelerated wax accumulation compared with controls. Ethephon accelerated and AVG inhibited .alpha.-farnesene accumulation.

CC 11-3 (Plant Biochemistry)
IT **77-52-1**, Ursolic acid 502-61-4, .alpha.-Farnesene 54990-88-4, Cutin
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(developmental changes of cuticular constituents assocd. with ethylene during fruit ripening of 'Delicious' apples)
IT **77-52-1**, Ursolic acid
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(developmental changes of cuticular constituents assocd. with ethylene during fruit ripening of 'Delicious' apples)
RN 77-52-1 HCAPLUS
CN Urs-12-en-28-oic acid, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:157347 HCAPLUS
DOCUMENT NUMBER: 128:221456
TITLE: Skin care compositions containing a polycyclic triterpene carboxylic acid and a retinoid
INVENTOR(S): Granger, Stewart Paton; Scott, Ian Richard
PATENT ASSIGNEE(S): Chesebrough-Pond's USA Co., USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5723139 | A | 19980303 | US 1996-721878 | 19960927 |
| WO 9813019 | A1 | 19980402 | WO 1997-EP5139 | 19970918 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9747755 | A1 | 19980417 | AU 1997-47755 | 19970918 |
| AU 714984 | B2 | 20000113 | | |
| BR 9712135 | A | 19990831 | BR 1997-12135 | 19970918 |
| CN 1237897 | A | 19991208 | CN 1997-199920 | 19970918 |
| EP 975319 | A1 | 20000202 | EP 1997-910309 | 19970918 |
| EP 975319 | B1 | 20030402 | | |
| R: CH, DE, ES, FR, GB, LI | | | | |
| JP 2000503030 | T2 | 20000314 | JP 1998-515236 | 19970918 |
| RU 2175546 | C2 | 20011110 | RU 1999-108678 | 19970918 |
| CZ 289876 | B6 | 20020417 | CZ 1999-1088 | 19970918 |
| ZA 9708658 | A | 19990326 | ZA 1997-8658 | 19970926 |

KR 2000048698 A 20000725 KR 1999-702653 19990327
PRIORITY APPLN. INFO.: US 1996-721878 A 19960927
WO 1997-EP5139 W 19970918

OTHER SOURCE(S): MARPAT 128:221456

AB A polycyclic triterpene carboxylic acid in combination with either retinol or retinyl ester resulted in a synergistic inhibition of **keratinocyte** differentiation. The effects of polycyclic triterpene carboxylic acids in combination with retinol or retinyl ester were analogous to the treatment with retinoic acid. Combination of 2.5x10-9 M retinol and 10-6 M glycyrrhizic acid repressed **keratinocyte** TG1 to 45% of control levels, therefore acted synergistically to repress **keratinocyte** differentiation in an analogous manner to the effect of retinoic acid. An water in oil emulsion contained retinol 0.5, fully hydrogenated coconut oil 3.9, ursolic acid 5, Brij 92 5, bentone 38 0.5, MgSO4 7H2O 0.3, butylated hydroxy toluene 0.01, perfume and water q.s. 100%.

IC ICM A61K007-48
NCL 424401000
CC 62-4 (Essential Oils and Cosmetics)
Section cross-reference(s): 1

IT **Skin**
(**keratinocyte**, differentiation of; skin care compns. contg. polycyclic triterpene carboxylic acid and retinoid)

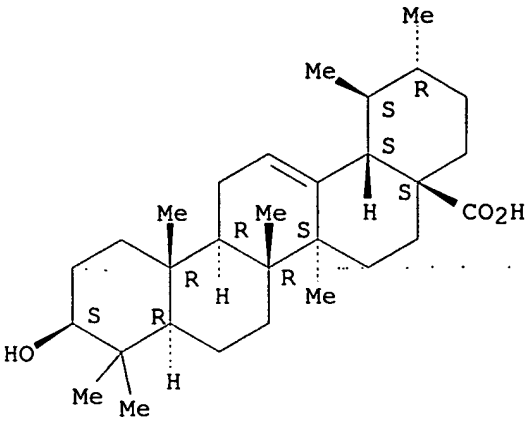
IT Cell differentiation
(**keratinocyte**; skin care compns. contg. polycyclic triterpene carboxylic acid and retinoid)

IT 68-26-8, Retinol **77-52-1**, Ursolic acid 79-81-2, Retinyl palmitate 127-47-9, Retinyl acetate 471-53-4, Glycyrrhetinic acid; 508-02-1, Oleanolic acid 631-89-0, Retinyl linoleate 1405-86-3, Glycyrrhizic acid 7069-42-3, Retinyl propionate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(skin care compns. contg. polycyclic triterpene carboxylic acid and retinoid)

IT **77-52-1**, Ursolic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(skin care compns. contg. polycyclic triterpene carboxylic acid and retinoid)

RN 77-52-1 HCAPLUS
CN Urs-12-en-28-oic acid, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).




REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:508125 HCAPLUS
DOCUMENT NUMBER: 117:108125
TITLE: Low molecular weight solutes in desiccated and ABA-treated calli and leaves of Craterostigma plantagineum
AUTHOR(S): Bianchi, Giorgio; Gamba, Anna; Murelli, Carla; Salamini, Francesco; Bartels, Dorothea
CORPORATE SOURCE: Exp. Inst. Elaiotec., Pescara, 65100, Italy
SOURCE: Phytochemistry (1992), 31(6), 1917-22
CODEN: PYTCAS; ISSN: 0031-9422
DOCUMENT TYPE: Journal
LANGUAGE: English

AB C. plantagineum, a resurrection plant, displays extreme desiccation-tolerance; dehydrated leaves and ABA-treated calli resume a normal metabolic state upon rehydration. Samples of calli and leaves of C. plantagineum were analyzed for the major classes of compds. such as sugars, fatty acids, amino acids and derivs., and phytosterols. Calli solutes are characterized by large amts. of glutamine and tyramine, triterpene acids and colneleic acid, an inhibitor of lipoxygenase. Among the sugars extd. from calli, sucrose, together with its hydrolytic products, predominates, while maslinic, ursolic and oleanolic acids are the most important triterpenes. In leaves the most common triterpene alcs. were campesterol, stigmasterol and .beta.-sitosterol. Almost 50% of the wt. of the lyophilized material consisted of 2-octulose, a sugar present as a minor component in a limited spectrum of plant species. Acquisition of desiccation tolerance in ABA-treated and desiccated calli was accompanied by an **increase** of **fatty** acids, accumulation of colneleic acid and by the disappearance of glucose and fructose. The most relevant biochem. effect of desiccation on leaves was the conversion of 2-octulose into sucrose.

CC 11-1 (Plant Biochemistry)

IT 50-99-7, Glucose, biological studies 51-67-2, Tyramine 56-41-7, Alanine, biological studies 56-85-9, Glutamine, biological studies 57-10-3, Hexadecanoic acid, biological studies 57-11-4, C18:0, biological studies 57-50-1, Sucrose, biological studies 57-88-5, Cholesterol, biological studies 60-33-3, 9,12-Octadecadienoic acid

(Z,Z)-, biological studies 61-90-5, Leucine, biological studies 72-19-5, Threonine, biological studies 73-32-5, Isoleucine, biological studies **77-52-1**, Ursolic acid 83-46-5, .beta.-Sitosterol 83-48-7, Stigmasterol 87-52-5, Gramine 87-89-8, Myoinositol 111-02-4, Squalene 111-62-6 112-05-0, Nonanoic acid 112-80-1, 9-Octadecenoic acid (Z)-, biological studies 112-85-6, Docosanoic acid 143-07-7, Dodecanoic acid, biological studies 320-77-4, Isocitric acid 463-40-1 464-99-3, Lupane 471-62-5, Hopane 474-62-4, Campesterol 502-69-2, 6,10,14-Trimethyl-2-pentadecanone 506-30-9, Eicosanoic acid 508-02-1, Oleanolic acid 544-63-8, Tetradecanoic acid, biological studies 557-59-5, Tetracosanoic acid 559-70-6, .beta.-Amyrin 621-82-9, Cinnamic acid, biological studies 628-97-7 638-95-9, .alpha.-Amyrin 640-43-7D, Abietane, derivs. 1136-86-3, 3'-4'-5'-Trimethoxyacetophenone 1191-41-9 1406-18-4, Vitamin E 2553-17-5, 9-Oxo-nonanoic acid 4373-41-5, Maslinic acid 5749-44-0, Kauran-13-ol 6915-15-7, Malic acid 9013-06-3, Octulose 28039-99-8 52761-34-9, Colneleic acid
RL: BIOL (Biological study)
(in desiccated and ABA-treated callus and leaves of Craterostigma plantagineum)

IT **77-52-1**, Ursolic acid
RL: BIOL (Biological study)
(in desiccated and ABA-treated callus and leaves of Craterostigma plantagineum)

RN 77-52-1 HCAPLUS

CN Urs-12-en-28-oic acid, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).